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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,751	11/01/2001	Alan T. Remaley	15280-3931US	7562

7590 05/17/2005

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EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,751	REMALEY ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 22, 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

Examiner acknowledges Applicants' Response, filed February 22, 2005, which amended claims 1-3, 5, 8-9, and cancelled claims 22-29. Claim 7 was withdrawn from consideration in the Office Action dated December 1, 2004, as being drawn to a non-elected species.

Currently, claims 1-6 and 8-21 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-6 and 8-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 4-6, 17 and 19, the recitation of "fraction" is indefinite because it is not clear whether/how a sample is fractioned or fractionated, or what mathematical operations are required for the determination of "fraction" or what physical parameters consist or comprise "fraction." In claim 1, the recitations of "fraction in the sample" or "fraction present in the sample" are indefinite because it is not clear whether/how said fractions are created, identified, isolated, separable, distinguishable, or is physically divided from the rest of the sample. In claim 1, the recitation of "a second lipoprotein fraction" is indefinite because it is not clear whether/how said second fraction is created, identified, isolated, separable, distinguishable, or is physically divided from the first lipoprotein fraction or from the rest of the sample. In addition, in claims 17 and 19, the recitation of "fraction consists of... in the sample" is indefinite because it is not clear how a fraction *consisting of* a particular lipoprotein can be created, identified, isolated,

separable, distinguishable, or is physically divided from a sample (e.g. serum, plasma) when the sample comprises lipoproteins and many other components.

In claim 1, step (b) the recitation of "a first cholesterol value" is indefinite because it is not clear how this value is used in the overall determination of cholesterol. The overall method of determining cholesterol does not appear to require "a first cholesterol value" after "a first cholesterol value" is obtained in step (b) and used to determine the amount of cholesterol in the first lipoprotein fraction in step (d). Therefore, its purpose is unclear.

In claim 1, step (d), it is not clear what steps are required for "determining the amount of cholesterol in the first and second lipoprotein fractions..." or whether "determining the amount of cholesterol in the first and second lipoprotein fractions..." requires the step of measuring the amount of cholesterol in the first and second lipoprotein fractions or why it is necessary to repeat the measurement of the amount of cholesterol in the second lipoprotein fraction, which was already performed in prior step (b).

In claims 10-11, the recitation of "the measuring of the amount of cholesterol present in steps (b) and (d) is performed by reacting... with cholesterol esterase" renders claim 1 indefinite. It is not clear how it is possible to measure the total amount of cholesterol in step (d) when an amount of cholesterol was already consumed by reaction with cholesterol esterase in step (b). Similarly, in claim 11, the recitation of "said cholesterol is reacted with cholesterol oxidase or cholesterol dehydrogenase" renders claim 1 indefinite because it is not clear how it is possible to measure the total amount of cholesterol in step (d) when an amount of cholesterol was already consumed by reaction with cholesterol oxidase or cholesterol dehydrogenase in step (b).

Claim Rejections - 35 USC § 102

Claims 1-6 and 8-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Miki et al. (US 6,162,607).

Miki et al. teach a method for determining amounts of cholesterol (see Abstract, "specifically for measuring the amount of cholesterol") in lipoprotein fractions (see col. 2, lines 62+, "any one of these lipoproteins can be selected as the specific lipoprotein to be the object of the measurement") in a sample (see Abstract, "serum and plasma") comprising the steps of: contacting a first lipoprotein fraction in the sample (see col. 6, line 15, "biological sample such as serum and/or plasma") with a complex-forming agent (see col. 6, line 16, "a first solution comprising an antibody reactive to lipoproteins(s)") to form a complex of said first lipoprotein fraction with the complex-forming agent (see col. 4, lines 1-4, "agglutination caused by the reaction of the antibody with lipoprotein(s)") wherein the complex is not a substrate for cholesterol esterase (see col. 3, lines 21-28, "The antibody... may include any one such as having an effect of preventing the objective constituents for measurement... from participating in the reaction with a reagent for measuring the amount of the objective constituents"), measuring the amount of cholesterol associated with a second lipoprotein fraction to obtain a first cholesterol value (see col. 2, lines 16-17, "measuring the absorbance (OD_1) of the reaction mixture"), dissociating the first lipoprotein fraction from the complex-forming agent (see col. 5, line 29-31, "The reagent solution containing no antibody (the 2nd solution)... further comprises a surfactant", (noting that the surfactant of Miki et al. necessarily causes dissociation of the first lipoprotein fraction from the complex forming agent, and would be so recognized by persons of ordinary skill in the art. *See e.g.* col. 5, lines 64-57, "when the surfactant is added to the first solution, measurement error caused by the objective constituent contained in lipoproteins other than the specific lipoprotein may be observed")), and measuring the total amount of cholesterol present in the sample (see col. 2, lines 20-21, "measuring again the absorbance (OD_2) of the latter reaction mixture").

With respect to claims 2-3, Miki et al. teach a method for determining amounts of cholesterol wherein the complex is not a substrate for cholesterol oxidase or cholesterol dehydrogenase (see col. 3, lines 21-28,

"The antibody... may include any one such as having an effect of preventing the objective constituents from measurement... from participating in the reaction with a reagent for measuring the amount of the objective constituents").

With respect to claim 4, Miki et al. teach a method for determining amounts of cholesterol wherein said first lipoprotein fraction is HDL-C (see col. 3, line 39, "anti-apolipoprotein A").

With respect to claim 5, Miki et al. teach a method for determining amounts of cholesterol wherein said first lipoprotein fraction is LDL-C (see col. 3, line 39, "anti-apolipoprotein B").

With respect to claim 6, Miki et al. teach a method for determining amounts of cholesterol wherein said complex-forming agent is an anti-lipoprotein antibody (see col. 3, lines 21-42).

With respect to claims 8-9, Miki et al. teach a method for determining amounts of cholesterol wherein a non-denaturing detergent deoxycholate is used (see col. 5, line 49, "deoxy cholic acid").

With respect to claims 10-11, Miki et al. teach a method for determining amounts of cholesterol wherein the measuring of the amount of cholesterol is performed by reaction with cholesterol esterase, cholesterol oxidase, or cholesterol dehydrogenase (see col. 4, line 63 to col. 5, line 4).

With respect to claim 12, Miki et al. teach a method for determining amounts of cholesterol wherein the first cholesterol value is subtracted from the total amount of cholesterol (see col. 2, line 25, "difference between OD_1 and OD_2").

With respect to claims 13-15, Miki et al. teach a method for determining amounts of cholesterol wherein an optical means is used to detect a dye indicator molecule (see col. 5, line 4, "nicotinamide adenine dinucleotide (NAD)").

With respect to claim 16, Miki et al. teach a method for determining amounts of cholesterol further comprising the step of determining the amount of any triglycerides (see col. 3, line 19).

With respect to claims 17-20, Miki et al. teach a method for determining amounts of cholesterol wherein the first lipoprotein fraction consists of apoB-containing lipoprotein or HDL-C (see col. 3, line 39, "anti-apolipoprotein A, anti-apolipoprotein B").

With respect to claim 21, Miki et al. teach a method for determining amounts of cholesterol wherein said antibody specifically binds to apoAI or apoAII (see col. 3, line 39, "anti-apolipoprotein A"). A person of ordinary skill in the art would recognize that the anti-apolipoprotein A antibody of Miki et al. would encompass either apoAI or apoAII.

Response to Arguments

In prior Office Action, claims 1, 4-6, 17 and 19 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "fraction." Specifically, the term "fraction" was considered indefinite because it was not clear how said fractions are created, identified, isolated, separable, distinguishable, or is physically divided from the rest of the sample or from other fractions. In response, Applicants' Remarks appear to point out that the recited "first lipoprotein fraction" and "second lipoprotein fraction" are distinguishable based on a differential interaction with the recited "complex-forming agent" among two species of lipoproteins (see Applicants' Remarks at p. 6, second full paragraph, lines 10-13, "the make-up of a particular lipoprotein faction is determined based on the species of lipoprotein(s) that can interact with a given complex-forming agent"). However, Applicants' invention, as claimed, does not allude to the existence of more than one species of lipoprotein. In addition, Applicants' invention, as claimed, does not allude to the notion that such a determination of "fraction" based on a differential interaction with the recited "complex-forming agent." Examiner considers such information as essential for an understanding

of Applicants' claimed method because a person skilled in the art may not be so imaginative as to import the clarifying details of Applicants' Remarks into the plain language of claim 1, as currently recited, and discern the organizational structure of a "fraction" based on a differential interaction with a complex-forming agent among two species of lipoproteins.

Applicants also observe that their invention, as claimed, does not require physical isolation, division, or separation of the fractions. Applicants' observation is noted.

In prior Office Action, claim 1 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "a first cholesterol value." In Applicants' Remarks, Applicants appear to concede that "a first cholesterol value" does not play a role in Applicants' invention (see Applicants' Remarks at p. 7, first full paragraph, line 11). Accordingly, the purpose of "a first cholesterol value" remains confounding.

In prior Office Action, claims 10-11 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "the measuring of the amount of cholesterol present in steps (b) and (d) is performed by reacting... with cholesterol esterase." In response, Applicants appear to point out that their invention requires absorbance-based measurements, which are accumulative (see Applicants' Remarks at p. 9, lines 1-4). However, Applicants' invention, as claimed, does not allude to absorbance-based measurements, and consequently, a person skilled in the art may not be so imaginative as to import the clarifying details of Applicants' Remarks into the plain language of claims 10-11, as currently recited, and discern "the accumulative nature of the absorbance-based method" (see Applicants' Remarks at p. 9, lines 3-4).

In prior Office Action, claims 1-6 and 8-21 were rejected under35 U.S.C. 102(e) as being anticipated by Miki et al. (US 6,162,607). In response, Applicants attempt to distinguish their invention from that of Miki et al. by pointing out that Miki et al. teach the measurement of only one "constituent" (see Applicants' Remarks at p. 10, first full paragraph, "the Miki et al. reference relates to a method for measuring the amount of a constituent (e.g. cholesterol) in only one lipoprotein fraction, but not the amount of the constituent in the remaining fraction"). On this issue, Applicants' argument is not persuasive because Applicants' invention, as claimed, also is limited to the measurement of only one "constituent." Similar to Miki et al., Applicants' invention, as claimed, appears to only recite a single "constituent" – a lipoprotein constituent (e.g. cholesterol).

In addition, Applicants argue that Miki et al. do not teach a method for measuring the total amount of cholesterol in a sample (see Applicants' Remarks at p. 10, last sentence, "Miki et al. reference does not teach how to determine... the total amount of cholesterol in the sample"). On this issue, Applicants' argument is not persuasive because Miki et al. teach a method wherein up to 10 w/v % surfactant is added (see col. 5, line 62) to a sample before measuring cholesterol. The addition of up to 10 w/v % surfactant necessarily results in measurement of the total amount of cholesterol in a sample, and would be so recognized by persons of ordinary skill in the art.

Conclusion

No claims are allowed at this time.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS

from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J Venci
Examiner
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